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From: David P. Halstead

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Date: December 20, 2001

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File Symbol: HMSU-P04-006

Personal ID Number: H28436

Submitted By: David P. Halstead

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Comments: **U.S. Application No.: 08/954,771****Filing Date: June 5, 1995****Group Art Unit: 1646****Examiner: M. Brannock****Title: Vertebrate Tissue Pattern Inducing Proteins and Uses Related Thereto**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Ingham et al.

Serial No: 08/462,386

Filed: June 5, 1995

For: Vertebrate Tissue Pattern Inducing
Proteins and Uses Related Thereto

Attorney Docket No. HMSU-P04-006

Art Unit: 1646

Examiner: M. Brannock

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I hereby certify that this correspondence is being transmitted by facsimile in the United States Patent and Trademark Office on the date indicated below:

December 20, 2001Date of Signature
and of Mail Deposit

Karen DiRocco

Assistant Commissioner of Patents
Washington, D.C. 20231

REPLY UNDER 37 CFR 1.111

Sir:

This amendment is being filed in reply to the outstanding Office Action, mailed September 24, 2001, in connection with the above application. Please enter the following amendments:

In the specification:

On page 142, please replace the last paragraph with:

Various fragments of the mouse *Shh* gene were cloned into the pET11D vector as fusion proteins with a poly(His) leader sequence to facilitate purification. Briefly, fusion genes encoding the mature M-*Shh* protein (corresponding to Cys-25 through Ser-437 of SEQ ID No. 11) or N-terminal containing fragments, and an N-terminal exogenous leader having the sequence M-G-S-S-H-H-H-H-L-V-P-R-G-S-H-M (SEQ ID No. 47) were cloned in pET11D and introduced into *E. coli*. The poly(His)-*Shh* fusion proteins were purified using nickel chelate chromatography according to the vendor's instructions (Qiagen catalog 30210), and the poly(His) leader cleaved from the purified proteins by treatment with thrombin.